Review of Human Rabies Prophylaxis and Treatment

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KEYWORDS

• Rabies • Rabies virus • Rabies vaccine • Lyssavirus
• Human rabies immune globulin • Antivirals • Immunizations • Human rabies

KEY POINTS

- Rabies is an acute, progressive encephalitis caused by a mammalian virus and carries with it an associated mortality of close to 100%.
- When used appropriately, postexposure prophylaxis after exposure to the rabies virus is universally effective.
- Postexposure prophylaxis involves adequate wound care, infiltration of rabies immune globulin, and vaccine administration.
- The treatment of human rabies infection is largely palliative, because no therapy has been shown to be effective.

INTRODUCTION

Rabies is an acute, progressive encephalitis caused by a group of RNA viruses that use mammals as reservoirs.[1,2] Although worldwide, rabies results in the deaths of more than 55,000 people annually, rabies is uncommon in developed nations.[3–8] One of the factors that makes this virus so unique is its associated mortality of close to 100% when prophylactic measures are not undertaken in an appropriate time frame. Fewer than 2 deaths are reported each year in the United States, down from more than 100 per year at the beginning of the twentieth century.[9] In addition to significant improvements in animal control, this decrease is in large part a result of the availability of postexposure prophylaxis, which has been proved to be almost 100%

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effective when used appropriately. However, this decrease in mortality comes at a significant cost to the health care system through its requisite time intensity and investment of substantial monetary resources; postexposure prophylaxis is complex, lengthy, and costly.[10] The estimated public health costs associated with disease prevention, detection, and control exceed $300 million in the United States annually.[11] Therefore, because of the high risk of mortality and the large financial investment that the US health care system has put toward the protection of the public from this devastating virus, it is imperative that all health care practitioners become familiar with the appropriate prevention of this disease and are prepared to implement aggressive treatment should the need arise.

TRANSMISSION

The neurotropic viruses that cause rabies are RNA viruses with multiple genotypes of the family Rhabdoviridae and genus *Lyssavirus*.[2,12–14] All rabies strains in North America are of genotype 1. Lyssaviruses move through the peripheral nervous system to their target, the central nervous system (CNS), where replication occurs.[15] From the brain, the virus travels to other organs or glands, such as the salivary glands, where it is excreted abundantly. This excretion of the virus may precede, be simultaneous, or occur after the development of clinical signs and symptoms. The rabies virus is not viable outside the host and can be inactivated by sunlight, heat, and desiccation.[16] As a result, exposure must occur when there is penetration of the skin by teeth or, less commonly, through direct transdermal or mucosal contact. The most common and important route of transmission is through infected saliva after a bite.[17]

All mammals are susceptible and can transmit the rabies virus, but the primary reservoir worldwide is carnivorous mammals, including dogs and foxes, as well as bats.[18] In North America, raccoons and skunks also serve as important reservoirs. Technically, all mammals are susceptible to infection, but there is great interspecies variability with regards to being important reservoirs. Dogs are the major reservoir and vector worldwide for this virus, causing most human deaths each year.[19] However, canine vaccination programs and control of stray animals have greatly reduced the cases of domestic animal rabies in the United States, with dog rabies declining 90% in the last decade.[18,20] Subsequently, wild animals are the most important potential source of infection for both humans and domestic animals in the United States. In 2011, wild animals represented 91.8% of the rabid animals reported.[21] In the same year, most cases of rabies occurred among raccoons (32.8%), skunks (27%), bats (22.9%), and foxes (7.1%). Since 2002, 87.5% of naturally acquired, indigenous human rabies cases in the United States have resulted from variants of rabies viruses associated with bats.[18,21]

In the last 50 years, few nonbite exposures have been documented in humans.[22] Only 51 cases have been described in the literature as not being transmitted as the result of animal bites.[23–25] Most of the reported cases were caused by inadequately inactivated vaccine. Potential does exists for infection to occur through inhalation of the virus, although this may be possible only in research settings during the manipulation of tissue, because there is 1 documented case. Inhalation transmission can also occur in caves where bat density is high and minimal ventilation exists, as documented by 2 cases in Texas for which other plausible explanations exist.[22,26] Infrequently, human-to-human transmission has been reported. In 2004, 4 transplant recipients in the United States became infected from an infected organ donor, all resulting in the deaths of the organ recipients.[18,27,28] There is only 1 report of a human with encephalitic rabies biting another human.[29] In this case, the individual received